Amendments to the Specification:

On page 1, between line 1 and 2, directly after the title, please insert the following paragraph:

-- This is the U.S. national stage of International application PCT/EP2003/02289, filed March 6, 2003 designating the United States and claiming priority to European application 02005186.8, filed March 8, 2002. --

On page 1, between lines 2 and 3, please insert:

-- FIELD OF THE INVENTION —.

On page 1, between line 9 and 10, please insert:

-- BACKGROUND OF THE INVENTION —

On page 3, between line 7 and 8, please insert:

-- BRIEF SUMMARY OF THE INVENTION --

On page 4, please amend the paragraph starting on line 29 as follows:

-- The VEGF variants according to the invention may also have a signal sequence. The signal sequence may be connected N-terminally to the amino acid chain of the VEGF variant and have the sequence

Met Asn Phe Leu Ser Trp Ser Val His Trp Ser Leu Ala Leu
Leu Leu Tyr Leu His His Ala Lys Trp Ser Gln Ala. (SEQ ID No. 3)

On page 5, between line 16 and 17, please insert the following paragraph and headings:

-- BRIEF DESCRIPTION OF THE DRAWINGS

Figures 1, consisting of Figure 1A and 1B, shows that the $VEGF_{165}$ mutations are resistant to cleavage by plasmin. The figure shows incubation of $VEGF_{165}$ and the mutated proteins in a plasmin solution [0.01 U/ml] or buffer solution (Figure 1B, lanes 18, 19) for the stated periods. Analysis of the degradation behaviour took place by Western blotting and immunodetection.

Figures 2A to 2C show that the Ala_{111} to Pro_{111} mutation increase the stability of VEGF in chronic wound fluid. Figure 2A: $VEGF_{165}$ wild type expressed in COS-1 cells. Figure 2B: the VEGF variants were incubated in chronic wound fluid for the stated periods, and the degradation behaviour was visualized by immunodetection. In this case, wound fluids from two different patients were investigated: patient X, lanes 1-16; patient Y: lanes 17-20). Figure 2C: Densitometric visualization of the degradation of VEGF wild type and $Mut_{Lys\text{-}Pro}$ in chronic wound fluid. The relative signal strength from three independently performed Western blot analyses (mean +/- SD) is shown.

Figure 3 shows that the VEGF mutants are biologically active. $VEGF_{165}$ wild type and VEGF mutants were each incubated in increasing concentrations with HUVE cells. The rate of incorporation of the base analogue into the DNA of the proliferating cells determined by BrdU ELISA is shown (mean +/- SD; n=3).

Figures 4A to 4D show that plasmin does not alter the biological activity of the $VEGF_{165}$ mutants. A comparison is shown of the relative BrdU incorporation into HUVE cells through stimulation with $VEGF_{165}$ wild type (Figure 4A, Figure 4B), Mut_{Ala} (Figure 4C) and $Mut_{Lys\text{-}Pro}$ (Figure 4D) after incubation of the stated protein in buffer or plasmin (means +/- SD; n=3).

Description of Various and Preferred Embodiments of the Invention --.

On page 6, please amend the paragraph starting on line 6 as follows:

-- Four mutants were produced by site-directed mutagenesis by carrying out targeted amino acid replacements at Arg_{110} and Ala_{111}. The cDNA which codes for human $VEGF_{165}$ was cloned into the SV40 replication expression vector pcDNA 3.1 (from Invitrogen, De Schelp, NL) using the BamHI and EcoRI cleavage sites in the cloning site. The Gene Editor™ system from Promega (Mannheim) was used for the site-directed in vitro mutagenesis. This system is based on annealing of oligonucleotides which harbour the appropriate mutation onto the initial sequence. The initial sequence of $VEGF_{165}$ in the region of the mutations is:

106 107 108 109 110 111 112 113

GA CCA AAG AAA GAT AGA GCA AGA CAA G (SEQ ID No. 4)

Pro Lys Lys Asp Arg Ala Arg Gln (SEQ ID No. 5) --

On page 6, please amend the paragraph starting on line 21 as follows:

-- Mutation 1: Mut_{Ala}:

GA CCA AAG AAA GAT *GCC* GCA AGA CAA G (SEQ ID NO. 6)

Pro Lys Lys Asp *Ala* Ala Arg Gln (SEQ ID NO. 7)

On page 6, please amend the paragraph starting on line 25 as follows:

-- Mutation 2: Mut_{Gln}:

GA CCA AAG AAA GAT *CAG* GCA AGA CAA G (SEQ ID No. 8)

Pro Lys Lys Asp *Gln* Ala Arg Gln (SEQ ID No. 9) --

On page 6, please amend the paragraph starting on line 29 as follows:

-- Mutation 3: Mut_{Pro}:

GA CCA AAG AAA GAT AGG *CCA* AGA CAA G (SEQ ID No. 10)

Pro Lys Lys Asp Arg *Pro* Arg Gln (SEQ ID No. 11) --

On page 7, please amend the paragraph starting on line 2 as follows:

-- Mutation 4: $Mut_{Lys\text{-}Pro}$:

GA CCA AAG AAA GAT *AAG CCA* AGA CAA G (SEQ ID No. 12)

Pro Lys Lys Asp *Lys Pro* Arg Gln (SEQ ID No. 13) --

On page 7, please amend the paragraph starting on line 18 as follows:

-- $VEGF_{165}$ wild type: $-Asp_{109}Arg_{110}Ala_{111}Arg_{112}-$ (SEQ ID No. 14)

Mut_{Gln}: $-Asp_{109}Gln_{110}Ala_{111}Arg_{112}-$ (SEQ ID No. 15)

Mut_{Ala}: $-Asp_{109}Ala_{110}Ala_{111}Arg_{112}-$ (SEQ ID No. 16)

Mut_{Pro}: $-Asp_{109}Arg_{110}Pro_{111}Arg_{112}-$ (SEQ ID No. 17)

$Mut_{Lys\text{-}Pro}$: $-Asp_{109}Lys_{110}Pro_{111}Arg_{112}-$ (SEQ ID No. 18) --

On page 13, please delete the paragraphs starting on line 21 and 26.

On page 14, please delete the paragraphs starting on line 2 and 7.

On page 15, please delete the first line and insert therefore:

-- WHAT IS CLAIMED IS: --